tagonist (either BQ610, ET-A selective, or bosentan, nonselective) 10^{-7}M or and/or exogenous ET-1 10^{-9}M. H + R stimulated ET-1 release (521 ± 177 mean ± SD pmol/plate vs 114 ± 13 pmol/plate after nonhypoxic incubation (NH), P < 0.006). Activity of eNOS (^{3}Harg-cit conversion with stimulation by A23187) was progressively impaired by 60–180 min of hypoxia. Activity of eNOS after 60 or 180 min H + R was preserved by both ET antagonists and worsened by exogenous ET. The % of nonviable cells (trypan blue exclusion) after 180 min H + R was similarly decreased by ET antagonists and increased by ET vs CON. PKC activity in membrane fractions was additively increased by ET and by H + R, and markedly reduced by BQ610 after 180 min H + R vs CON. Nonviability after 180 min H + R was increased by addition of PMA 10 nM vs CON. Activity of eNOS after 60 and 180 min H + R was preserved after PKC downregulation by 24 hours of PMA 100 nM. Endogenous and exogenous ET-1 promote hypoxic injury and eNOS impairment in this in vitro model, possibly via PKC. This action of ET may contribute to endothelial dysfunction following ischemia/hypoxia and in other disorders characterized by endothelial dysfunction.

986-80 A Long-acting Nitric Oxide Donor Suppresses Basal and LPS-Stimulated Tissue Factor Procoagulant Activity in Human Monocyte-derived Macrophages

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Endothelium-derived nitric oxide (NO) contributes to the thromboresistance of normal arteries by inhibiting platelet-endothelium interaction. The effect of NO on the expression of tissue factor, a macrophage-derived procoagulant glycoprotein detected in atherosclerotic plaque, is unknown. Therefore, we determined the effect of a long-acting ($t_{1/2}$ = 20 hrs) diazeniumdiolate NO donor (DETA/NO, 100 μM) on basal as well as on lipopolysaccharide (1 μg/ml) stimulated tissue factor expression in human monocyte-derived macrophages. This was accomplished using a procoagulant assay based on a standard clotting time curve utilizing recombinant human TF. Viability was 85–93% as assessed by trypan blue exclusion

Results: DETA-NO reduced basal procoagulant activity by 64% (0.1 ± 0.17 ng/10^6 cells vs 0.28 ± 0.21 ng/10^6 cells; p < 0.02, n = 11). Lipopolysaccharide increased PCA by 360% (1.29 ± 1 ng/10^6 cells vs 0.28 ± 0.21 ng/10^6 cells) and DETA-NO attenuated this effect by 47% (p = 0.03). Tissue factor protein as evaluated by densitometry-analyzed Western blot was increased 7.5-fold from basal level after lipopolysaccharide stimulation and DETA-NO attenuated this response by 59%.

Conclusion: Suppression of basal and Lipopolysaccharide-stimulated tissue factor protein and PCA in monocyte-derived macrophages by DETA-NO suggests yet another mechanism by which endothelium-derived NO may exert an antithrombotic effect in the vessel wall.

986-81 L-Arginine Attenuates the Impairment in Exercise Capacity due to Hypercholesterolemia

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Background: We have shown that hypercholesterolemia impairs exercise capacity in mice and that this may be due to altered nitric oxide-mediated vascular function. The following study was performed to determine whether dietary supplementation with L-arginine attenuates this impairment.

Methods and Results: Eight week old wild type (*E+*) and apoE deficient (*E–*) C57BL/6J mice were divided into groups with and without L-arginine supplementation (*A;* 6 g/100 ml drinking water). At the beginning of the study, and again after a 14 week period, the mice were treadmill-tested to measure parameters defining exercise capacity (maximal oxygen uptake (V_{O2max}), anaerobic threshold (AT), aerobic work capacity (AWC), and change in distance run to exhaustion (ΔDISTe)). At eight weeks of age, parameters defining exercise capacity were similar in both wild type and apoE mice. By 22 weeks of age, exercise capacity had improved in the wild type mice; by contrast, exercise capacity deteriorated in the apoE mice. L-arginine supplementation reduced a 20% difference in V_{O2max} between wild type and apoE mice to 10%, reduced a 25% difference in AT to 9%, and reduced a 32% difference in AWC to no difference from controls. L-arginine completely prevented the decline in running distance observed in apoE mice.

Conclusion: This study demonstrates that L-arginine reverses the decline in exercise capacity observed in hypercholesterolemic mice.

Exercise Capacity in 22 Week Old Mice

Group	n	VO2max	AT ml O_2/min/kg	AWC J/g	DISTe m
E+	16	135 ± 3	114 ± 2	6.6 ± 0.6	17 ± 20
E–	15	108 ± 3**	86 ± 2**	4.5 ± 0.4	–190 ± 20**
AE+	13	140 ± 4	107 ± 5	8.2 ± 2.	19 ± 32
AE–	8	121 ± 2*	98 ± 3*	8.4 ± 1.**	120 ± 65**

*p < 0.05, **p < 0.001 (E– vs E+ and AE– vs E–) by ANOVA

987 Peripheral Vascular Disease

Tuesday, March 18, 1997, 9:00 a.m.–11:00 a.m.
Anaheim Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

987-90 Long-Term Incidence of Restenosis After Carotid Endarterectomy and Results of Reoperation

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Documentation of the long-term outcome of carotid endarterectomy in regard to vessel re-stenosis or thrombosis rates is important both for patient (pt) management and as a baseline for comparison with newer approaches to carotid disease such as stenting. We evaluated 2686 pts, mean age 63.9 (21–90) yrs, 70% male operated upon between 1953 and 1994 who underwent 3495 carotid endarterectomies. Follow-up angiography was performed on 655 pts with 780 operated carotid arteries. Restenosis >50% was identified in 71/780 (9.1%) arteries at a mean interval of 60.7 ± 60.7 months, range 0–248 months. Occlusion was found in 67/780 (9.0%) arteries at a mean interval of 30.8 ± 33.2 mths, range 0–141 mo. The total annual rate of occlusion or restenosis (Kaplan-Meier) was 1.3%. Multivariate analysis demonstrated that younger age at operation, smoking, obesity and hypertension were independent predictors of restenosis/occlusion. Reoperation was performed in 41 pts: 37 for recurrent neurological symptoms and asymptomatic high grade stenosis in 4 pts. There were 46 procedures: 43 carotid re-endarterectomy and patch angioplasty; 2 saphenous vein interposition and 1 Dacron interposition graft. Post op there was 1 (2.4%) mild and 1 (2.4%) severe (fatal) stroke for periop mortality of 2.4%. Restenosis occurrence after the second carotid surgery was 2/41 (2.9%) at 84 mths, range 8–22 mths. Thus the long-term durability of carotid surgery is excellent but a subgroup of pts at high risk of restenosis/occlusion has been identified. Reoperation is an effective approach for treatment of restenosis in selected cases.

987-91 Retinal Vascular Abnormalities in Patients with Coronary Artery Disease

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We investigated the relationship between coronary artery disease (CAD) and retinal vascular abnormalities in 51 pts subjected to selective coronary angiography and to retinal fluoroangiography. Automatic quantitative analysis of coronary arteriograms was performed to assess the presence and number of stenoses determining a lumen narrowing greater than 50%. Digital quantitative analysis was applied to retinal fluoroangiograms to determine the fluorescence-time curve, the presence of peripapillar fluorescence and the presence of optik disk ischemia (ODI). The severity of ODI was also evaluated semiquantitatively by assigning a score from 0 to 3. Patients with diabetes or hypertension were excluded. *Results:* 21 patients showed normal coronary angiograms (group A) whereas 30 patients showed significant coronary stenoses (group B). The time to fluorescin choroidal flush and the fluorescin transit time were significantly longer in group B with respect to group A (63 ± 13 vs 13 ± 5 sec, p < 0.01 and 99 ± 31 vs 49 ± 13 sec, p < 0.01, respectively). Peripapillar fluorescence was observed in 26 out of 30 patients of group B (87%) but only in 2 out of 21 patients of group A (10%) (p < 0.001). Similarly, ODI was observed in 27 out of 30 patients of group B (90%) and in 2 out of 21 patients of group A (10%) (p < 0.001). The semiquantitative score of ODI was significantly correlated to the number of stenosed coronary vessels (r = 0.463, p < 0.03). *Conclusions:* patients with CAD show a high incidence of retinal vascular alterations. Such alterations, when detected, might represent a sensitive marker for an otherwise unsuspected CAD.